

the teachings of which are incorporated herein in their entirety). The choice of framework residues can be critical in retaining high binding affinity. In principle, a framework sequence from any human antibody can serve as the template for CDR grafting; however, it has been demonstrated that straight CDR replacement into such a framework can lead to significant loss of binding affinity to the antigen (Tempest *et al.*, *Biotechnology* 9: 266 (1992); Shalaby *et al.*, *J. Exp. Med.* 17: 217 (1992)). The more homologous a human antibody is to the original murine antibody, the less likely the human framework will introduce distortions into the mouse CDRs that could reduce affinity. Based on a sequence homology, III2R (SEQ ID NOS: 25, 29) was selected to provide the framework for the humanized 3D1 heavy chain and H2F (SEQ ID NOS: 26, 30) for the humanized 3D1 light chain variable region. Manheimer-Lory, A. *et al.*, *J. Exp. Med.* 174(6):1639-52 (1991). Other highly homologous human antibody chains would also be suitable to provide the humanized antibody framework, especially kappa light chains from human subgroup 4 and heavy chains from human subgroup 1 as defined by Kabat.

**IN THE CLAIMS:**

Please amend the claims as follows:

- C2
1. (Twice Amended) A method of inhibiting the interaction of a first cell bearing a B7-2 receptor with a second cell bearing B7-2, comprising contacting said second cell with an effective amount of a humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising:
- a) at least one antigen binding region of nonhuman origin and
  - b) at least a portion of an immunoglobulin of human origin derived from the III2R (SEQ ID NOS: 25, 29) and/or the H2F (SEQ ID NOS: 26, 30) variable region,

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U.S. Patent  
P. 21/1500

wherein the immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the III2R (SEQ ID NOS: 25, 29) and/or the H2F (SEQ ID NOS: 26, 30) antibody and the humanized immunoglobulin has a binding affinity of at least about  $10^7$  M<sup>-1</sup>.

2. (Twice Amended) A method of inducing immunotolerance in a patient having a transplanted organ, tissue, cell, or the like comprising administering an effective amount of a humanized immunoglobulin having binding specificity for B7-2, said immunoglobulin comprising:

- a) at least one antigen binding region of nonhuman origin, and
- b) at least a portion of an immunoglobulin of human origin derived from the III2R (SEQ ID NOS: 25, 29) and/or the H2F (SEQ ID NOS: 26, 30) variable region,

wherein the immunoglobulin is administered in a carrier, and wherein the immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the III2R (SEQ ID NOS: 25, 29) and/or the H2F (SEQ ID NOS: 26, 30) antibody and the humanized has a binding affinity of at least about  $10^7$  M<sup>-1</sup>.

3. (Twice Amended) A method of reducing transplantation rejection in a patient having a transplanted organ, tissue, or cell, comprising administering a therapeutically effective amount of a humanized antibody having binding specificity for B7-2, said immunoglobulin comprising:

- a) at least one antigen binding region of nonhuman origin, and

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b) at least a portion of an immunoglobulin of human origin derived from the III2R (SEQ ID NOS: 25, 29) and/or the H2F (SEQ ID NOS: 26, 30) variable region,

wherein the immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the III2R (SEQ ID NOS: 25, 29) and/or the H2F (SEQ ID NOS: 26, 30) antibody and the humanized immunoglobulin has a binding affinity of at least about  $10^7$  M<sup>-1</sup>.

C3  
6. (Amended) The method of claim 1, wherein said at least one antigen binding region further comprises at least one CDR of the variable region of the 3D1 (SEQ ID NOS: 21, 23) antibody.

10. (Amended) The method of claim 1, wherein said immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the III2R (SEQ ID NOS: 25, 29) antibody.

C4  
11. (Amended) The method of claim 1, wherein said immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the H2F (SEQ ID NOS: 26, 30) antibody.

12. (Amended) The method of claim 2, wherein said at least one antigen binding region further comprises at least one CDR of the variable region of the variable region of the 3D1 (SEQ ID NOS: 21, 23) antibody.

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C5  
16. (Amended) The method of claim 2, wherein said immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the III2R (SEQ ID NOS: 25, 29) antibody.

17. (Amended) The method of claim 2, wherein said immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the H2F (SEQ ID NOS: 26, 30) antibody.

C6  
22. (Amended) The method of claim 3, wherein said immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the III2R (SEQ ID NOS: 25, 29) antibody.

23. (Amended) The method of claim 3, wherein said immunoglobulin has at least a portion of the amino acid sequence of its variable region in common with at least a portion of the amino acid sequence of the variable region of the H2F (SEQ ID NOS: 26, 30) antibody.

**REMARKS**

**STATUS OF THE CLAIMS**

Claims 1-26 are pending. Claim 5 has been withdrawn from further consideration by the Examiner as being drawn to a non-elected invention. Claims 1-4 and 6-26 are currently under consideration.

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